UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,096	05/02/2006	Rosario Lizio	282276US0PCT	7191

22850 7590 02/22/2010

OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
WESTERBERG, NISSA M	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
02/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/564,096
Filing Date: May 02, 2006
Appellant(s): LIZIO ET AL.

Teddy S. Gron
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 20, 2009 appealing from the Office action mailed June 22, 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US 6,465,626	WATTS	10-2002
US 5,849,327	BERLINER	12-1998
US 5,773,032	ENGEL	06-1998
EP 1203590	SHIMONO	05-2002

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

A. Claims 1, 3, 6 – 11 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. (US 6,465,626).

Watts et al. discloses compositions comprising chitosan, type A gelatin and a therapeutic agent (col 3, ln 7 – 10). The compositions are in the form of microparticles (col 3, ln 61 – 65), whose diameter are between 1 to 200 μm (col 5, ln 39 – 42). A variety of therapeutic agents, including a number of peptides and proteins some having a molecular weight less than 3,000 Da, are disclosed as suitable for use in the compositions (col 5, ln 65 – col 6, ln 17). Other ingredients such as absorption enhancers can be included in the compositions and compounds which act as absorption enhancers include phospholipids (col 7, ln 64 – 67). The compositions can be

formulated in a variety of dosage forms that are familiar to those skilled in the art such as tablets, capsules and pellets (col 6, ln 52 – 67). A tablet or capsule formed using the micropellet results in an oral multiparticulate dosage form.

While the preferred route of administration of the compound is nasal (col 7, ln 5), the compounds can also be administered orally and the pellets adapted for delivery of the therapeutic agent to the small intestine or colon (col 7, ln 10 – 13). This is preferably done through techniques known to those skilled in the art such as coating dosage forms with enteric polymers (col 7, ln 14 – 25). Among such polymers are those polymers sold under the trade name EUDRAGIT® (col 7, ln 22 – 25). The enteric polymer prevents release of the therapeutic environment in the stomach which is more acidic, but the coating dissolves upon exposure to the less acidic environment of the small intestine (col 7, ln 19 – 22). The site of delivery may also be controlled by the varying the thickness of the polymer coating (col 7, ln 46 – 49). Pages 18 and 19 of the instant specification discloses the monomeric content of various EUDRAGIT® polymers and the composition of the polymers are anionic (meth)acrylate polymers with an anionic monomer content of 5 – 60 wt% and which also dissolve in the pH from 4.0 to 8.0 in the intestine.

In the examples (beginning on col 9, ln 1), microspheres comprised of chitosan, gelatin A and therapeutic peptides (insulin in examples 1 and 2, salmon calcitonin (SCT) in examples 3 and 4 and parathyroid hormone (PTH) in example 9) are prepared. The amount of active ingredient present in the composition varies depending on the active ingredient being used and were all well below the 40% maximum amount of active

ingredient recited in claim 1 (3.6 wt% for insulin, 0.2 wt% for SCT and 0.4% for PTH). The pH of the layer comprising the chitosan and active ingredient was adjusted to 4 by means of the acid HCl (e.g., col 9, ln 10 – 11). The optimal pH for a particular component depends on the formulation being used and the properties of the active agent being used. For example, if the peptide active ingredient was subject to acid hydrolysis at low pH, a higher pH would be used to mitigate breakdown of the active ingredient during formulation. Thus the pH of a composition is a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal pH in order to best achieve the desired results.

As to the physical properties such as the viscosity and water uptake of the mucoadhesive polymer, chitosan is exemplified by Applicant as a polymer having these properties.

A specific example of a peptide with a molecular weight less than 3,000 Da having all the properties as described in the claims was not prepared.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a composition as recited by the instant claims as the various elements and generally conditions are described by Watts et al. as discussed in much greater detail above. The teachings of a document are not limited to the specific

examples and the elements of the claims are disclosed by Watts et al., rendering the claims of the instant application obvious.

B. Claims 1, 3, 4, 6 – 11 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. as applied to claims 1, 3, 6, 7, 8, 10 and 11 above, and further in view of Berliner et al. (US 5,849,327).

As discussed above, Watts et al. discloses a pharmaceutical composition of pellets comprised of chitosan and a peptide or protein active ingredient. To prevent release of the active ingredient in the stomach when administered orally, an enteric coating may be applied and the thickness of the layer varied to alter the location in which the active ingredient is released by altering the time it takes to dissolve the enteric and expose the layer containing the active ingredient.

Watts et al. does not disclose the physical thickness of the layers that can be applied.

Berliner et al. discloses a oral dosage forms that are coated with an enteric coating (abstract). The coating thickness may vary but in general, coating thicknesses of about 0.1 to about 1.0 mm (100 μm – 1,000 μm) provide the best results (col 4, ln 66 – col 5, ln 3).

It would have been obvious to one of ordinary skill in the art to apply an enteric coating of the thickness of 100 μm – 1,000 μm taught by Berliner et al. to the compositions taught by Watts et al. which comprise chitosan, a protein or peptide active ingredient and an enteric coating. Watts et al. discloses that such coatings are well

known to those skilled in the art (col 7, ln 14 – 16) and Berliner et al. teaches that variations in the thickness of this layer alter the portion of the digestive system in which the active ingredient is released.

C. Claims 1, 3, 4, 6 – 11 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. as applied to claims 1, 3, 6, 7, 8, 10 and 11 above, and further in view of Engel et al. (US 5,773,032).

As discussed above, Watts et al. discloses a pharmaceutical composition of pellets comprised of chitosan and a peptide or protein active ingredient. To prevent release of the active ingredient in the stomach when administered orally, an enteric coating may be applied and the thickness of the layer varied to alter the location in which the active ingredient is released by altering the time it takes to dissolve. A variety of therapeutic agents are disclosed including LHRH (luteinising hormone releasing hormone) and analogs such as nafarelin, buserelin, leuprolide and goserelin (col 6, ln 3 – 5). The exemplified compounds are short (≤10 amino acids) peptidic analogs of LHRH.

Watts et al. does not explicitly disclose cetrorelix as suitable therapeutic agent.

Engel et al. disclose the decapeptide cetrorelix is a LHRH antagonist (analog; col 1, ln 25 – 26; col 2, ln 1 – 4). Also listed as LHRH antagonists are goserelin (col 1, ln 33 – 34) and leuprolide (col 1, ln 42 – 43).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a composition comprising a therapeutic active agent and

chitosan and coated with an enteric polymer layer as taught by Watts et al. using cetrorelix as the therapeutic agent as cetrorelix is taught as LHRH analog by Engel et al. The substitution of cetrorelix as the active ingredient in the compositions of Watts et al. is obvious because Watts et al. discloses the genus of compounds to which cetrorelix, as well as specific peptidic compounds of the same length as cetrorelix, as suitable for use in the composition, making these various active ingredients functionally equivalent in that they are all LHRH antagonists.

D. Claim 34 was rejected under 35 U.S.C. 102(b) as being anticipated by Shimono et al. (EP 1203590).

Shimono et al. discloses a nonpareil that is coated the active ingredient, chitosan and EUGRAGIT® RS that are prepared in example 6 (col 12, ln 39 – 55). This layer is then coated with the 50% methylmethacrylate, 50% methacrylic acid EUDRAGIT® L to give a particle with a diameter of 1.4 mm (example 7, col 13, ln 1 – 11). Together the non-pareil, chitosan, active ingredient and EUDRAGIT® RS form the inner matrix of the composition and there is no layer separating those ingredients from the outer coating of EUDRAGIT® L. No ingredient identified as a mucoadhesive lipophilic matrix is present in the inner matrix. The outermost coating is an enteric polymer that meets the pH limitations of claim 34, as a copolymer of 50 wt% methylmethacrylate and 50wt% methacrylic acid exemplified for the outer coating material in dependent claim 35.

E. Claims 1, 4, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimono et al. (EP 1203590) in view of Watts et al. (US 6,465,626).

Shimono et al. discloses a nonpareil that is coated with a layer comprising chitosan and EUGRAGIT® RS that are prepared in example 6 (col 12, ln 39 – 55) that are further coated with the 50% methylmethacrylate, 50% methacrylic acid EUDRAGIT® L to give a particle with a diameter of 1.4 mm (example 7, col 13, ln 1 – 11).

Shimono et al. does not disclose the inclusion of cetrorelix as the active ingredient in the dosage from.

Watts et al. discloses compositions comprising chitosan, type A gelatin and a therapeutic agent (col 3, ln 7 – 10). The compositions are in the forms of microparticles (col 3, ln 61 – 65), whose diameter are between 1 to 200 μm (col 5, ln 39 – 42). Compositions of bioadhesive matrices with enteric coatings can be used to prevent release of the therapeutic agent until it reaches the small intestine or colon (col 7, ln 10 – 36). Among the active ingredients which can be delivered using such a deliver system is LHRH (lutensing hormone release hormone) and analogs such as nafarelin, buserein, leuprolide and goserelin (col 6, ln 3 – 5). The peptide/protein active ingredients are embedded in the chitosan/gelatin matrix for delivery to the small intestine or colon.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare the sustained release dosage form comprising an inner chitosan containing layer with an enteric coating layer utilizing a methacrylic acid/methacrylate polymer such as EUDRAGIT® L as taught by Shimono et al. and to

embed in the inner matrix layer a protein/peptide active ingredient, as taught by Watts et al. Shimono et al. demonstrates that microcapsules with this release profile need not be constructed with an inner matrix containing gelatin and can be made using chitosan without gelatin.

F. Claims 1, 4, 9, 10 and 33 – 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimono et al. and Watts et al. as applied to claims 1, 4, 33 and 34 above, and further in view of Engel et al. (US 5,773,032).

Shimono et al. and Watts et al. disclose multiparticulate pharmaceutical forms with an inner matrix comprising active substance and chitosan. The active substance can be small molecules such as acetaminophen (Shimono et al.) or a variety of therapeutic peptide/proteins such LHRH (luteinising hormone releasing hormone) and analogs of LHRH such as leuprolide and goserelin (col 6, ln 3 – 5 of Watts et al.) which are all short (≤10 amino acids) LHRH analogs.

Watts et al. does not explicitly disclose cetrorelix as a suitable therapeutic agent.

Engel et al. disclose the decapeptide cetrorelix as a LHRH antagonist (analog; col 1, ln 25 – 26; col 2, ln 1 – 4). Also identified as LHRH antagonists are goserelin (col 1, ln 33 – 34) and leuprolide (col 1, ln 42 – 43).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a composition comprising a therapeutic active agent and chitosan and coated with an enteric polymer layer as taught by Shimono et al. and Watts et al. and to use cetrorelix as the therapeutic agent. Engel et al. teaches that

cetrorelix is a LHRH analog and is therefore functionally equivalent to the LHRH analogs taught by Watts et al. as suitable for inclusion in the multiparticulate formulations taught by Shimono et al. and Watts et al.

G. Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Applicants have discussed that the composition may contain a lipophilic matrix which has a melting point above 37°C in which the active ingredient is embedded, which is then embedded in the matrix of the polymer with a mucoadhesive effect (see original claim 20). Applicants do not, however, disclose anything in regards to "a mucoadhesive lipophilic matrix embedded in the inner matrix" as the disclosure relates to a lipophilic matrix IN the mucoadhesive matrix. As the component has not been disclosed, the ingredient cannot be excluded from the compositions as claimed.

H. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection of the limitation excluding

gelatin from the inner matrix layer. The only mention of "gelatin" in the specification is that the pellets of the pharmaceutical formulation can be placed in a gelatin capsule (lines 20 – 21, p 33 of the instant specification). This does not provide sufficient support for a limitation regarding the composition of the inner matrix layer of the pellets.

(10) Response to Argument

A. Claims 1, 3, 6 – 11 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. (US Patent 6,465,626).

Appellants discuss the meaning of and differences between bioadhesive materials (e.g., gelatin) and mucoadhesive materials. Claim 1, in part, is drawn to a product which have an inner matrix layer consisting essentially of a mucoadhesive polymer having a mucoadhesive effect in which is embedded a peptide or protein active substance. In claim 34, the inner matrix comprising an active pharmaceutical ingredient and a polymer having a mucoadhesive effect. For claim 1, the transitional phrase "consisting essentially of" closes the inner matrix layer to those materials that materially affect the basic and novel characteristics of the claimed invention as a matter of law. This argument is unpersuasive. The specification of the instant application teaches that the compositions are useful for the delivery of pharmaceutically active ingredients following oral administration. This is the same activity described by Watts et al. for its compositions. The addition of gelatin to this composition may alter the particular delivery

properties, but does not change or "materially affect" the delivery of pharmaceutically active ingredients following oral administration. Thus, gelatin is not excluded from the instant claims by the transitional phrase "consisting essentially of".

For claim 34, Appellants argue that the inner matrix is functionally closed to matrix-forming materials in amounts which change the polymer having a mucoadhesive effect into a polymer NOT having a mucoadhesive effect. It is unreasonable, in light of the invention disclosed in the specification to read on an inner matrix layer which does not include a polymer exhibiting a mucoadhesive effect. This argument is unpersuasive. The preamble of the claim and the section regarding the inner matrix all use the completely open language of "comprising". There is no requirement in the claim that the dosage form as a whole be bioadhesive or mucoadhesive, only that a polymer having a mucoadhesive effect with particular physical properties is present. Chitosan is one such polymer having those properties (see the Markush group of claim 1).

It is the difference in transitional phrases that should cause claim 1 and its dependent claims to be considered separately from claim 34 and its dependent claim. As shown above, the transitional phrases of these two claims are both being interpreted as open language.

Appellant argues that the evidence of record indicates that bioadhesive polymeric mixtures which comprise minor amounts of chitosan do not comprise a polymer having a mucoadhesive effect. Polymers having a mucoadhesive effect bind to mucus or mucin whereas bioadhesive polymers bind to the mucosal membrane. This causes things

which bind to the mucoadhesive membrane to bind strongly and continuously to internal tissues whereas those which bind to mucus or mucin are readily and regularly eliminated from the body, reducing the risk of toxicity from prolonged exposure to the active substance in the polymer. Watts' pellets provide for the target release of a bioadhesive inner matrix as acknowledged by Watts and the evidence of record as a whole. Watts also disclose enteric coating to prevent release of the therapeutic agents in the stomach. Most importantly Watts found improved presentation (may gel on the mucosa to at least some extent to facilitate retention of the composition on the mucosa) of vaccines to mucosal surfaces over the results obtained from chitosan or type A gelatin alone. The present invention is designed not to be retained at the mucosal surface. No polymers in Watts' compositions have a mucoadhesive effect and that combination of at least 50% gelatin and at most 50% chitosan binds to and is retained by the mucosal surface. When not combined with gelatin, chitosan does exhibit a mucoadhesive effect but not when combined with gelatin, as then the chitosan appears to have a bioadhesive effect. Neither compositions as recited in claim 1 or 34 are reasonably suggested by Watts. Watts does not recognize the problems associated with strong mucosal binding bioadhesive polymers and contrarily would have lead persons having ordinary skill in the art to believe that stronger and longer binding to the mucosal membrane is better, leading away from Applicant's invention.

These arguments are unpersuasive. In both claims 1 and 34, the inner matrix must include a polymer having a mucoadhesive effect, of which chitosan is one examples of a polymer with the requisite properties. In claim 1, the last subsection

states "wherein the polymer having a mucoadhesive effect" has certain physical properties and is chosen from a Markush group which include chitosan, not that the inner matrix layer or the multiparticulate pharmaceutical form have those properties the physical properties at the end of the claim only modifies the mucoadhesive polymer having a mucoadhesive effect. Whether the dosage form as a whole is bioadhesive or mucoadhesive is not relevant as those features are not recited in the instant claims. As the cited prior art does not covalently modify the chitosan with gelatin, it is the position of the Examiner that the simple mixing of chitosan with gelatin will not alter the physical properties of the chitosan so as to render the chitosan non-mucoadhesive and/or not have the mucoadhesive effect and water uptake as recited by the instant claims. Appellants have not provided any evidence as to this change in properties to the chitosan itself, and not in relationship to the layer or composition as a whole. The prior art need not appreciate the problem which Applicant identified and does not teach away as those features which Applicants relied upon for the teaching away are not recited in the instant claims.

B. Claims 1, 3, 4, 6 – 11 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al, further in view of Berliner et al. (US 5,849,327).

Berliner does not remedy the deficiencies of Watts. Berliner does not disclose or reasonably suggest a coating thickness appropriate for coating an inner matrix including an active peptide or protein ingredient and a mucoadhesive polymer having a mucoadhesive effect. There is insufficient factual basis for the rejection in the absence some teaching, suggestion, incentive and/or motivation to combine.

These arguments are unpersuasive. Watts is not deficient regarding the mucoadhesive polymer as discussed above. As taught by Berliner et al., one of ordinary skill in the art would optimize the thickness of the layers of the dosage form of Watts et al. in order to vary the release location of the active ingredient, making the layer thickness a results effective parameter that one of ordinary skill in the art would optimize.

C. Claims 1, 3, 4, 6 – 11 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. further in view of Engel et al. (US 5,773,032).

Appellant states that Engel is cited by the Examiner for its disclosure of the active ingredient cetrorelix in a sustained release particulate form. However, Engel does not remedy the other deficiencies of Watts' disclosure. Engel does not disclose or reasonably suggest making and using pharmaceutical pellets comprising an inner matrix including cetrorelix and a mucoadhesive polymer having a mucoadhesive effect. Unless there is some suggestion, teaching, incentive, and/or motivation to combine Engel's teaching with Watts' disclosure to produce an oral multiparticulate pharmaceutical pellets including an inner matrix comprising an active ingredient such as cetrorelix and a polymer having a mucoadhesive effect, there is insufficient factual basis for the rejections over the combined prior art disclosures. Moreover, neither Watts, Engel, nor any combination thereof reasonably suggests preparing Applicant's claimed compositions using cetrorelix as the active ingredient with a reasonable expectation that

cetrorelix would or could be made compatible with the other components of the claimed invention and released as required by Claim 1.

These arguments are unpersuasive. As discussed above, Watts is not deficient in regards to the limitations on the mucoadhesiveness of the compositions being claimed. Watts et al. discloses that peptidic, LHRH analogs can be included in such compositions and are compatible with the other components of the composition and Engle discloses that cetrorelix is also a peptidic LHRH analog, rendering cetrorelix functionally equivalent to the active agents discloses as suitable for use in the compositions by Watts et al. As all of the agents have the same function and are peptide active ingredients, one of ordinary skill in the art would have a reasonable expectation of success in being able to prepare such a dosage form.

D. Claim 34 was rejected under 35 U.S.C. 102(b) as being anticipated by Shimono et al. (EP 1203590).

The teachings of Shimono et al. indicate that the medicament-containing core is not present in an inner matrix comprising the medicament and chitosan, but rather that the medicament is separated from the chitosan by an inner matrix of water-insoluble polymer. As interpreted in light of the specification, the inner matrix must comprise and include both the active substance and the chitosan and Shimono does not describe or reasonably suggest that the two active materials may be combined in a single inner matrix layer. It is unreasonable to interpret the phrase "inner matrix comprising" to broadly encompass inner matrices which do not contain active ingredients, as described

in Shimono. The configuration of Shimono also does not conform to the configuration of the claimed invention as the water-insoluble polymer layer not only contains dispersed chitosan particles but separates the medicament containing layer from the outer enteric coating. This argument is unpersuasive. The inner matrix does not need to contain only a single layer as there was no such definition in the specification as originally filed. The medicament, water-insoluble polymer and chitosan of form together form the inner matrix. As the enteric coating is directly applied to the water-insoluble polymer and chitosan containing layer, no layer separating the inner matrix and outer coating is present. Thus, the configuration as required by the instant claims is taught by Shimono.

Appellant also argues that the description in Shimono of making the surface of membranes in the large intestine more porous suggests that the chitosan particles bind to the mucosal membrane and thus are bioadhesive, not mucoadhesive. The persons having ordinary skill in the art would expected the compositions to have bioadhesive and not mucoadhesive properties, and the mucoadhesive properties appear to be negated by the inclusion of the water-insoluble polymers as the sustained release properties which would require that the preparations be retained in the intestine and not readily eliminated or flushed from the system. As discussed in greater detail above, the instant claims only require that a polymer having a particular mucoadhesive effect and water uptake, not the inner matrix or composition as a whole have those properties. It is the position of the Examiner that embedding of chitosan particles in a water-insoluble polymer will not alter the physical properties of the chitosan so that the chitosan no

longer has the required mucoadhesive effect and water uptake. Appellants have not presented any evidence that this is not the case.

Appellant also argues that because of the water-insoluble polymer, the mixture will be very slow to dissolve and is unlikely to occur in the required 15 minutes at the neutral to acid intestinal levels required in claim 34. This argument is unpersuasive. Claims 34 only requires that outer coating, not the whole pellet, dissolve within 15 – 60 minutes at pH ranging from 5.5 to 7.2. Appellant's argument without factual support is a mere allegation which is not found persuasive.

E. Claims 1, 4, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimono et al. (EP 1203590) in view of Watts et al. (US 6,465,626).

Shimono is directed to a sustained release composition comprising a core coated with a water-insoluble polymer in which is dispersed particles of chitosan with an outer, enteric coating layer. On the other hand, Watts relates to compositions with an inner matrix of at least 50% gelatin and no more than 50% chitosan, with the preponderance of evidence on the record showing that such a matrix does not consist essentially of an active substance and a mucoadhesive polymer having a mucoadhesive effect. The preponderance of evidence also shows that having the mucoadhesive effect or water uptake as required by either claim 1 or 34. The Office has not provided any evidence that the compositions of either reference is a mucoadhesive polymer or comprises a polymer having, exhibiting or providing a inner matrix with a mucoadhesive effect. These arguments are unpersuasive. As discussed in greater detail above, the instant

claims only require that a polymer having a particular mucoadhesive effect and water uptake, not the inner matrix or composition as a whole have those properties. Therefore, the Office does not need to provide any such evidence.

Appellant also argues that Shimono does not suggest including a peptide or protein, particular cetrorelix, as required by claims 6 – 8 and 35. This argument is unpersuasive as claims 6 – 8 and 35 are not rejected over this combination of prior art.

The Examiner has also not established the existence of common relationship or proper between Watts' gelatin and Shimono's water-insoluble polymer which would have led persons having ordinary skill in the art to reasonable believe that any elements of Shimono's compositions or Watts' could be replaced. This argument is unpersuasive. Watts et al. is cited for its teaching that peptide active ingredients can be delivered using multi-layered orally administered, dosage forms having an outer enteric layer and an inner matrix containing chitosan and the active ingredient. Exact equivalent of all the ingredients in the composition is not required in order for the references to be combinable.

The Examiner summarily finds that chitosan is chitosan and thus inherently carries its mucoadhesive properties and benefits to any and all compositions including chitosan at all times. The evidence of record clearly indicates that this is erroneous. Watts' compositions of gelatin and chitosan are bioadhesive while the compositions of Shimono are sustained release which attach to a mucosal membrane. Shimono also does not suggest including a peptide or protein medicament in an inner matrix, particularly the cetrorelix as required by claims 6 – 8 and 35. Most importantly, neither

reference discloses an inner matrix consisting essentially of as required by claim 1. The Examiner points to no evidence to contradict the evidence relied upon by Appellant in support of the patentability of the claims. These arguments are unpersuasive. Whether or not the inclusion of gelatin and/or water-insoluble polymers changes the layer or composition as a whole from mucoadhesive to bioadhesive is not relevant as those properties are not claimed. As chitosan is exemplified as a polymer have the requisite mucoadhesive effect, the presence of chitosan in the inner matrix layer meets the limitations set forth in the claims regarding the mucoadhesive polymer.

F. Claims 1, 4, 9, 10 and 33 – 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimono et al. and Watts et al. further in view of Engel et al. (US 5,773,032).

Appellants argue that the problem with Examiner's rationale is that no combination of Shimono and Watts would have led to the claimed delivery compositions and without some guidance, teaching, incentive or motivation to combine cetrorelix with a mucoadhesive polymer having a mucoadhesive effect, persons having ordinary skill in the art would have had no reason to make and use the claimed form with any reasonable expectation of success. These arguments are unpersuasive. The lack of deficiencies of Shimono and Watts are discussed in the previous section and Appellant provides no additional arguments regarding Engel.

G. Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Appellant states that they Examiner's fining is erroneous because at page 37, line 35 is a paragraph heading of "Lipophilic matrix/polymers having a mucoadhesive effect". A mucoadhesive inner matrix clearly is disclosed and its inclusion in the inner matrix is preferred, leading persons having ordinary skill in the art to understand that the mucoadhesive lipophilic matrix can be embedded in the inner matrix or may be excluded from the inner matrix.

These arguments are unpersuasive. In looking at the paragraph which follows the heading, it is clear that "lipophilic matrix/polymers having a mucoadhesive effect" refers to two separate items, a lipophilic matrix and polymers having a mucoadhesive effect, as these two items when present in the composition would preferably have the same ionic properties, although if these materials are of opposed ionic properties, the polymer having a mucoadhesive effect should be presented in the neutralized form (p 38, ln 1 – 12). There is no indication that the slash is being used as shorthand to refer to the items lipophilic matrix having a mucoadhesive effect and lipophilic polymers having a mucoadhesive effect, which would be required for the former term to provide sufficient written description for the limitation "mucoadhesive lipophilic matrix" and thereby support by which that item could be excluded from the claimed compositions.

H. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Appellant states that while the disclosure does not expressly describe a composition that does not contain gelatin in its inner matrix layer, the specification

positively teaches that the claimed pellets may be packed into gelatin capsules. The specification also provides a wealth of examples in which the inner matrix of the pellets does not contain gelatin. Literal description is not required and the test is one of if the specification reasonably conveys to the artisan that the inventor had possession at the time of filing of the later claimed subject matter. The disclosure irrefutably shows possession, including compositions where the inner matrix does not contain gelatin. New words in the claims do not justify a finding of new matter. Gelatin is positively disclosed in the specification exclusively for its used in encapsulating the claimed pellets, which would be reasonably understood by persons having ordinary skill in the art that gelatin may be excluded from every element of the claimed invention but the outermost encapsulating layer.

These arguments are unpersuasive. While gelatin capsules serve to encapsulate the pellets of the pharmaceutical formulations, this is a distinct concept from the layers which are used to encapsulate individual pellets within the capsule. While Appellants have written description support for the specific formulations in the specification that do not contain gelatin, those examples are insufficient to support the exclusion of gelatin from all formulations, just as the specification would not support a limitation such as the pharmaceutical form does not contain eye of newt, even though none of the examples contain eye of newt.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Nissa M Westerberg/

Examiner, Art Unit 1618

Conferees:

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612